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Baruch Blumberg (1925–2011)

"It is clear that I could not have planned the investigation at the beginning to find the cause of hepatitis B. This experience does not encourage an approach to basic research which is based exclusively on specific goal-directed programs for the solution of biological problems".

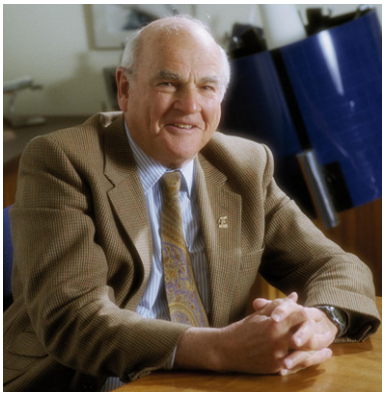
Nobel Lecture, December 13, 1976

The initial steps of a scientific career may teach more on the process who leads a researcher to unanimously recognized discoveries than any speculation on the chance he may have benefited. Born in 1925, Baruch Blumberg had the first of his many field experiences in the late forties when, during his medical studies, he went to Sumatra where he cared for a remote pluriethnic population and became interested in the heterogeneous response of this population to infection. *"This experience was recalled in later years when I became interested in the study of inherited variations in susceptibility to disease"* he said. Following a fellowship in rheumatology, he joined the Oxford University Department of Biochemistry where he did his PhD thesis on the properties of hyaluronic acid. During this period, he was introduced to the concept of polymorphism and began studying, in various populations, inherited polymorphisms of serum proteins in relation to disease. He followed this research line from 1957 to 1964 as head of the Geographic Medicine and Genetics Section at NIH and, subsequently, created the Division of Clinical Research of the Institute for Cancer Research (ICR) in Philadelphia where he was appointed Professor of Medicine and Anthropology at the University of Pennsylvania.

Performing fieldwork all over the world, his research was marked by an integrated pluridisciplinary approach, which was reflected by the skills of members of his research group (notably T. London, I. Millman, E. Lutsbader, and B. Werner) and his many close collaborations with immunologists, virologists, clinicians, pathologists, epidemiologists, and anthropologists.

Among the many outstanding scientists who deciphered the unique molecular mysteries of HBV at Fox Chase ICR (retrovirus in disguise, hepaDNA genus replication, cccDNA, etc.), one must mention Jessie Summers, Bill Mason, Christoph Seeger, John Tailor (HDV), without forgetting Bob Snyder who first described the HBV hepatocellular cancer model in woodchucks.

The year 1964 marked the beginning of his improbable hepatitis B saga. In the early 1960, he tested the hypothesis that "*Patients who had received large numbers of transfusions might develop antibodies against one or more of the polymorphic serum proteins, which themselves had not inherited*". By means of a simple double gel diffusion technique, he and his group used the serum of polytransfused patients to screen sera from many different populations. In 1963, he observed a precipitin band between the serum of a hemophilia patient from New York and that of an Aborigine from Australia. He coined this presumed polymorphism "Australia Antigen" (Au), which showed wide geographical distribution variations with higher frequency in patients with leukemia or Down Syndrome. By early 1966, one of the trisomic patients he was following up with E. Sutnick and W. London turned Au-positive while originally Au-negative. "*We did a series of liver chemistry tests which showed that between the first (negative for Au) and the second testing (positive for Au); the patient had developed a form of anicteric hepatitis*". Serendipitously, this sequence also occurred in a lab technician. This initial publication coauthored by Harvey Alter [1] who indeed had initially observed the new antigen for the first time generated much skepticism. But the association between Au and hepatitis was soon confirmed by further studies especially from K. Okochi in Japan and A.M. Prince in the US, who rightly associated it specifically with hepatitis B only.



Dr. Baruch Blumberg (1925–2011) (*Image credit:* NASA/Tom Trower)

The consequences of this discovery were immediate and immense. As early as 1969, blood banks worldwide began screening blood donors for Au (later on renamed HBsAg). In the late 1960s, K. Okochi demonstrated that transfused patients were much less likely to develop post transfusion hepatitis if they received an Au-positive unit and/or developed antibodies against it (anti-HBs).

"*We presumed that the very large amount of HBsAg present in the blood could be separated from any infectious particles and used as an antigen to elicit the production of antibodies*" which "*in turn would protect against infection by the virus*". The revolutionary concept of the first generation hepatitis B "plasma vaccine" was born, the first ever antiviral vaccine which was not obtained via *in vitro* cultivation. This paved the way, after the cloning of HBV by P. Tiollais in Paris, to the development of the present engineered recombinant vaccines now integrated worldwide in the universal vaccine agenda for newborns. Blumberg's group

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also contributed to the development of serological tests, to the description of the natural history of hepatitis B and of its geographical distribution, to the importance and ethical implications of mother–child transmission in the spread of the HBV carrier state, and finally, in collaboration with French and Senegalese research groups, to its role in hepatocellular carcinoma. Many more steps of his career would deserve to be mentioned. Last but not least the well deserved Nobel Prize in Medicine in 1976. Those who knew him were not surprised when, in 1999, he was appointed director of NASA's Astrobiology Department, looking for the origin of life. Still highly active, he died in California preparing for a lecture.

The driving energy, curiosity, and creativity describe at best and in a few words, the distinctive nature of Barry Bloomberg, the man, (for a while excellent squash player). Within his group in the Department of Clinical research, he was always capable of integrating, without partisanship, all specialties in a common project of truly pluridisciplinary dimensions.

His group, in his image, was most welcoming and in the frequent weekly "protocol" meetings, new ideas emerged, always very innovating and even sometimes utopist and ultimately wrong but amazingly creative. During his research visits in the field, occasionally quite exotic, he recognized the spirit of his own work. He owed his humanity to his immense culture: literary as well as scientific and to his unique sense of humor.

When his intrusive landmark contributions in the closed field of leprosy were challenged by "the" experts, he ironized "*We are now lepers among lepers*".

Reference

[1] Alter H. Baruch Blumberg (1925–2011). Nature 2011;473 (7346), 155.

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